An evolutionary arms race between KRAB zinc-finger genes ZNF91/93 and SVA/L1 retrotransposons.

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Authors: Frank M J Jacobs, David Greenberg, Ngan Nguyen, Maximilian Haeussler, Adam D Ewing, Sol Katzman, Benedict Paten, Sofie R Salama, David Haussler

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Public Summary:
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Scientific Abstract:
Throughout evolution primate genomes have been modified by waves of retrotransposon insertions. For each wave, the host eventually finds a way to repress retrotransposon transcription and prevent further insertions. In mouse embryonic stem cells, transcriptional silencing of retrotransposons requires KAP1 (also known as TRIM28) and its repressive complex, which can be recruited to target sites by KRAB zinc-finger (KZNF) proteins such as murine-specific ZFP809 which binds to integrated murine leukaemia virus DNA elements and recruits KAP1 to repress them. KZNF genes are one of the fastest growing gene families in primates and this expansion is hypothesized to enable primates to respond to newly emerged retrotransposons. However, the identity of KZNF genes battling retrotransposons currently active in the human genome, such as SINE-VNTR-Alu (SVA) and long interspersed nuclear element 1 (L1), is unknown. Here we show that two primate-specific KZNF genes rapidly evolved to repress these two distinct retrotransposon families shortly after they began to spread in our ancestral genome. ZNF91 underwent a series of structural changes 8-12 million years ago that enabled it to repress SVA elements. ZNF93 evolved earlier to repress the primate L1 lineage until approximately 12.5 million years ago when the L1PA3-subfamily of retrotransposons escaped ZNF93's restriction through the removal of the ZNF93-binding site. Our data support a model where KZNF gene expansion limits the activity of newly emerged retrotransposon classes, and this is followed by mutations in these retrotransposons to evade repression, a cycle of events that could explain the rapid expansion of lineage-specific KZNF genes.